EXHIBIT B

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF WEST VIRGINIA
CHARLESTON DIVISION

IN RE: ETHICON, INC., PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION	**Master File No. 2:12-MD-02327** **MDL 2327** **JOSEPH R. GOODWIN** **U.S. DISTRICT JUDGE**
THIS DOCUMENT RELATES TO: *Wave 4 Cases*	

EXPERT REPORT OF SAMANTHA J. PULLIAM, M.D.

TVT and TVT-O Expert Report of Samantha J. Pulliam, M.D

In the course of preparation of this report I have reviewed the medical and scientific literature concerning the efficacy and safety of TVT and TVT-O. I have reviewed position statements and guidelines from a variety of professional societies and other organizations. I have also reviewed the Ethicon TVT Instructions for Use, the Ethicon TVT-O Instructions for Use, the TVT Exact Instructions for Use, the TVT Abbrevo Instructions for Use, Professional Education materials made available to surgeons who place TVT and TVT-O devices, the Surgeons Resource Monograph, and other Ethicon documents. A list of these materials and those that I may use at trial are attached to this report.

The contents of this document contain my professional opinions I have formed to date, and a summary of the information I considered informing these opinions. In total, they are based on my years of experience, conversations with other professionals and colleagues, attendance at professional meetings, my review of the above literature, and my knowledge of science, medicine and surgery based on my training in the fields of biology, pathology, obstetrics and gynecology, and female pelvic medicine and reconstructive surgery.

All of the opinions expressed in this report are held to a reasonable degree of medical and scientific certainty. This report is based on the information I have at this time. To the degree I receive additional information, I may form additional opinions or some of my opinions may be modified.

Qualifications, Training and Experience

I am a sub-specialist in the field of Female Pelvic Medicine and Reconstructive Pelvic Surgery. My decision to pursue subspecialty training in this specialty stemmed from a desire to provide surgical correction for women with pelvic organ prolapse and stress urinary incontinence. I have been practicing since 2006 in some of the finest academic medical centers in the country including Massachusetts General Hospital and the University of North Carolina.

I am a Diplomate in the American Board of Obstetrics and Gynecology and I am board certified in both Obstetrics and Gynecology and Female Pelvic Medicine and Reconstructive Surgery. I was in the inaugural cohort of physicians specializing in Urogynecology to receive board certification in 2013, when the subspecialty assumed the current name, Female Pelvic Medicine and Reconstructive Surgery. I hold unrestricted licenses to practice medicine in North Carolina and Massachusetts.

Currently, I serve as the Division Director of Urogynecology at University of North Carolina Chapel Hill. In this capacity, I serve as the administrator of a dynamic division that includes seven Urogynecologists, as well as a multitude of staff, residents and fellows. I hold the academic title of Assistant Professor of Obstetrics and Gynecology.

I received my Doctor of Medicine Degree from Wake Forest University School of Medicine in 1998. After medical school, I spent much of my advanced training in the Boston area, in high volume academic centers with some of the most accomplished practitioners in my field. I completed my residency at the Combined OB/GYN program at Brigham and Women's Hospital and Massachusetts General Hospital (MGH). MGH was the home of Dr. David Nichols, a preeminent pelvic reconstructive surgeon, and I was privileged to train with Dr. May Wakamatsu, Dr. Arlan Fuller and Dr. Keith Isaacson, all leaders in vaginal, abdominal and laparoscopic surgery. I completed a fellowship in Female Pelvic Medicine and Reconstructive Surgery at Mt. Auburn Hospital in Cambridge, Massachusetts, under the supervision of Peter Rosenblatt, one of the early fellowship trained gynecologists who continues to lead in the innovative work still required to optimize therapies for women with pelvic floor disorders such as urinary incontinence. My education also included one year of internship at Massachusetts General Hospital in Anatomic Pathology, providing further depth in the basic science of pathology, which I have applied to my clinical practice of pelvic reconstructive surgery.

Throughout my professional career, I have been involved in maintaining and setting standards for the sub-specialty of Female Pelvic Medicine and Reconstructive Surgery at the national and international level through leadership in the American Urogynecologic Society. I currently serve as the Council Chair for Quality, overseeing the activity of the Quality Outcomes and Quality Network and Quality Registry Committees. This role has afforded me the opportunity to be engaged in the development of best practices to optimize quality outcomes and safety for women with pelvic floor disorders including urinary incontinence.

I currently serve as a peer reviewer for five premier gynecology medical journals: Female Pelvic Medicine & Reconstructive Surgery, American Journal of Obstetrics and Gynecology, Menopause, Journal of Minimally Invasive Gynecology, and the International Urogynecology Journal. I have authored dozens of scholarly journal articles, addressed hundreds of professional audiences on topics including urinary incontinence and pelvic disorders, including lectures about the appropriate use of mesh and new technologies in pelvic reconstructive surgeries.

My clinical research has included an evaluation of practice patterns with regard to mesh use in female pelvic medicine and reconstructive surgeons, as well as evaluations of the epidemiology of painful bladder syndrome, the cost-effectiveness of sling vs. pelvic floor physical therapy for treatment of stress urinary incontinence, and the evaluation of quality metrics for assessment of quality care for women undergoing pelvic reconstructive surgery and surgery to treat urinary incontinence.

Over the course of my career, I have performed thousands of gynecologic surgeries, specifically female pelvic floor reconstruction such abdominal, laparoscopic and robotic sacrocolpopexy, vaginal hysterectomy, high uterosacral ligament suspensions, sacrospinous ligament suspensions, native tissue repair, biologic graft and synthetic mesh augmented repairs.

I was trained to perform open and laparoscopic colposuspensions and paravaginal repairs, autologous fascial slings, and a variety of minimally invasive mid-urethral slings including retropubic (both abdominal approach and vaginal approach), obturator (so-called "inside out" and "outside in" approaches), and single incision slings by Dr Peter Rosenblatt, Dr. Eman Elkadry, and Dr. Anthony DiScuillo. I have performed more than 700 mid-urethral sling procedures over the past 10 years, predominantly retropubic and transobturator. Although I have performed slings using other brands of mid-urethral sling, the predominant types have been Gynecare/Ethicon TVT and TVT-Exact, as well as TVT-O and TVT-Abbrevo. During my fellowship training, I actively participated in Gynecare professional education and have trained other surgeons to use these products, including over 100 OB/GYN residents, 7 fellows, and additional Gynecologists and Urogynecologists. I have served as faculty in many types of professional activities such as cadaver labs, Ethicon training labs, and lectures. Along with a colleague, I currently hold a patent on a vaginal suspension procedure, and actively participate in the development of new technologies for the treatment of urinary incontinence and pelvic organ prolapse.

My career in academic medicine has included multiple teaching roles and activities. I served as the Associate Residency Director to a 40-resident at the premiere OB/GYN training program at Brigham and Womens'/Massachusetts General Hospital. I became the fellowship director for the first American Council for Graduate Medical Education fellowship training program in Female Pelvic Medicine and Reconstructive Surgery at Massachusetts General Hospital. I was responsible for the development and implementation of the curriculum for fellows including surgical training in the placement of mid-urethral slings.

For additional information please refer to my attached Curriculum Vitae.

Fees and Expert Testimony

My fees for serving as an expert in this matter are: $500/hour for record review, report drafting and meetings, and $600/hour for deposition and trial testimony. I have not given expert deposition or trial testimony in the prior four years.

Stress Urinary incontinence

- Definition

Stress urinary incontinence (SUI) is defined by the International Continence Society as the complaint of involuntary leakage of urine on effort or exertion, or on sneezing or coughing (Abrams, P. et al, The standardization of terminology of lower urinary tract function: report from the Standardization Sub-committee of the International Continence Society, Am J Obstet Gynecol. 2002 Jul;187(1):116-26).

- Prevalence

Stress urinary incontinence occurs in 15% women overall, and increases with age. In middle age women, one in four has stress urinary incontinence (Thom, D., Variation in Estimates of Urinary Incontinence Prevalence in the Community: Effects of Differences in Definition, Population Characteristics, and Study Type, J of Am Geriatrics Soc, 1998). By age 60, up to 31% of women experience leakage (Nygaard I. et al, Prevalence of symptomatic pelvic floor disorders in US women, JAMA. 2008;300(11):1311-1316). Leakage of urine in this manner can have far-reaching consequences, and can have a negative impact on a woman's quality of life. SUI can limit a woman socially, due to fear of leakage, and can have severe psychological consequences, even in intimate relationships. Limitations in the ability to exercise without leakage can decrease the level of physical activity, which can have long-term health consequences.

- Pathophysiology

The pathophysiology of SUI is not completely understood, but there are several theories which are commonly accepted as explanations for SUI. The Integral theory of incontinence, upon which the tension-free vaginal tape sling was based (TVT), states that SUI results from damage to the puborethral ligaments (Petros PE et al., The Integral Theory of continence, Int Urogynecol J Pelvic Floor Dysfunct. 2008 Jan;19(1):35-40). Damage (due to childbirth, chronic cough, obesity) sustained to the supportive tissue and muscle around the urethra (the tube where urine exits the bladder) results in insufficient support of the urethra. The result of this damage is that the urethra cannot completely close when compressed against the anterior vaginal wall. When there is an increase in intraabdominal pressure, the urethra does not close completely, and urine leaks out. A different theory, though with some similarities, is the hammock hypothesis which suggests that hypermobility of the bladder and urethra results in impaired pressure transmission to the urethra, ineffective urethral compression, and inefficient skeletal muscle response with the onset of increased intraabdominal pressure (Am J Obstet Gynecol 1994 170:1719).

Another form or cause of SUI is called intrinsic sphincter deficiency. This occurs when the urethra sustains neuromuscular damage, resulting in a loss of urethral tone. This type of damage results in severe leakage even with a very small increase in abdominal pressure, and can be more difficult to treat successfully.

- Cost

The economic impact of SUI is significant; both by reducing a woman's ability to engage in active work, and by the cost of pads and other devices intended to prevent leakage. Urinary incontinence, including SUI, is the second most common reason for nursing home admission, resulting in significant costs to the healthcare system. An ACOG/AUGS Practice Bulletin from November 2015 on Urinary Incontinence in Women estimated that the "direct cost of urinary incontinence care in the United States is $19.5 billion." (ACOG / AUGS Practice Bulletin No. 155; Nov. 2015.)

Risk factors SUI

- Obesity

Obesity is a leading risk factor, as obese women have nearly 3 times the odds of SUI compared with women who are not obese. The ACOG / AUGS Practice Bulletin No. 155; Urinary Incontinence in Women, Nov. 2015 states that obese women have a 4.2-fold greater risk of developing SUI compared to women with an average BMI. Several studies (observational) have demonstrated significant reductions in SUI following weight loss after bariatric surgery. (Bump, RC, et al., Obesity and lower urinary tract function in women: effect of surgically induced weight loss, Am J Obstet Gynecol. 1992 Aug;167(2):392-7; Subak LL, et al., Does weight loss improve incontinence in moderately obese women?, Int Urogynecol J Pelvic Floor Dysfunct. 2002;13(1):40-3). Pooling the results of two randomized controlled trials, obese women had higher scores on measures of incontinence severity including more frequent incontinence episodes, higher symptom distress, and greater impact on their quality of life (Richter, HE et al., The impact of obesity on urinary incontinence symptoms, severity, urodynamic characteristics and quality of life, J Urol. 2010 Feb;183(2):622-8).

- Pregnancy and childbirth

Increasing parity (giving birth to a larger number of children) is associated with stress urinary incontinence. This is due to damage to the muscles, nerves and fascia of the pelvis resulting from childbirth. Mode of delivery is also a factor, as vaginal delivery increases the risk of SUI. However, caesarian section is not completely protective, which suggests that pregnancy alone is a risk factor. When compared with cesarean delivery without labor, spontaneous vaginal birth was associated with higher odds of stress incontinence (OR 2.9 (95% CI, 1.5-5.5)) and prolapse at or beyond the hymen (OR 5.6 (95% CI, 2.2-14.7)) (Handa VL et al., Pelvic floor disorders after vaginal birth: effect of episiotomy, perineal laceration, and operative birth, 2012 Obstet Gynecol 2012; 119: pp. 233).

- Smoking

Women who smoke have been found to be up to 1.8–2.9 times more likely to develop SUI. (Bump RC, McClish DK. Cigarette smoking and urinary incontinence in women, Am J Obstet Gynecol. 1992 Nov;167(5):1213–1218).

- Menopause

Decreasing levels of estrogen that occur as menopause develops can lead to a weakening of endopelvic tissues in the vagina, and decrease the vascularity of the urethra and surrounding tissues.

- Pelvic organ prolapse

There is an association between pelvic organ prolapse and stress urinary incontinence, though this has not been established as causative. Approximately 2/3 of patients with stress urinary incontinence also have pelvic organ prolapse, while 2/3 of patients with pelvic organ prolapse have stress urinary incontinence (Siddighi S, Hardesty JS, Urogynecology & Female Pelvic Reconstructive Surgery, ISBN 0-07-144799-7).

- Exercise

There is an association between stress urinary incontinence symptoms and women who engage in high-impact exercise (Fozzatti, C, et al., Prevalence study of stress urinary incontinence in women who perform high-impact exercises, Int Urogynecol J. 2012 Dec;23(12):1687-91).

- Age

The average age of a woman with stress urinary incontinence is 48 years in the United States. In one study of non-pregnant women in the US, incontinence was reported to affect 3.5 percent of women ages 20 to 29, increasing to 38 percent of women age ≥80 years (Wu JM, et al., Prevalence and trends of symptomatic pelvic floor disorders in U.S. women, Obstet Gynecol. 2014 Jan;123(1):141-8), however, other studies suggest that it is comorbidities (such as obesity, birth history, menopause, and hormones) and not age account for this change over time (Lawrence JM, et al., Prevalence and co-occurrence of pelvic floor disorders in community-dwelling women, Obstet Gynecol. 2008 Mar;111(3):678-85).

- Genetics

While environmental variables such as vaginal deliveries and exercise have been shown to influence the development of stress urinary incontinence, there is also a genetic component that accounts for 40% of the liability for stress urinary incontinence (Altman D, et al., Genetic influence on stress urinary incontinence and pelvic organ prolapse. Eur Urol 2008;54(4):918–22).

- Race

The prevalence rates for SUI are higher among Caucasian women than African American women. One population based study showed the prevalence of SUI in Caucasian women in 39.2%, compared to 25% of African American women. Explanations for these racial differences are not clear, but may include genetic, anatomic or social factors (Fenner, DE, et al., Establishing the prevalence of incontinence study: racial differences in women's patterns of urinary incontinence, J Urol. 2008 Apr;179(4):1455-60).

Treatment of SUI

Non-surgical Treatment

Guidelines provided by all major societies affirm the value of non-surgical treatment of stress urinary incontinence, including scheduled voiding, fluid restrictions, smoking cessation, weight loss, pad use and pelvic floor muscle exercises (Syan, R. and Brucker, B. M. (2016), Guideline of guidelines: urinary incontinence. BJU Int, 117: 20–33. doi:10.1111/bju.13187). There are many non-surgical options for the treatment of SUI

- Pelvic floor exercises have long been a mainstay in the treatment of SUI, and may include home regimens, vaginal weights or cones, the assistance of pelvic floor physical therapists, or biofeedback to enhance the ability to squeeze the levator ani muscles.

- Weight loss has been shown to improve urinary incontinence. Women who undergo bariatric surgery report improvement in continence with loss of 40-50kg after bariatric surgery. Loss of as little as 5% of body weight by obese individuals can improve continence (Bump, RC, et al., Obesity and lower urinary tract function in women: effect of surgically induced weight loss, Am J Obstet Gynecol. 1992 Aug;167(2):392-7; Subak LL, et al., Does weight loss improve incontinence in moderately obese women?, Int Urogynecol J Pelvic Floor Dysfunct. 2002;13(1):40-3).

- Smoking cessation can improve SUI symptoms, both by diminishing the presence of toxins in the bladder, and by decreasing the frequency of chronic pulmonary conditions and chronic cough.

- Incontinence pessaries have been shown to reduce leakage of urine during exercise (Nygaard, I., Prevention of exercise incontinence with mechanical devices, J Reprod Med. 1995 Feb;40(2):89-94). Use of pessaries for this purpose has been accepted by many patients, with up to 59% continuing pessary use for incontinence after 1 year of use (Donnelly, MJ, et al., Vaginal pessaries for the management of stress and mixed urinary incontinence, Int Urogynecol J Pelvic Floor Dysfunct. 2004 Sep-Oct;15(5):302-7).

Surgical Treatments

- Anterior Colporrhaphy and Kelly Plication

Historically, Anterior Colporrhaphies and Kelly plications were some of the first surgical procedures to be used to address the problem of stress urinary incontinence. In 1914, Dr. HA Kelly described a procedure utilizing sutures placed beneath the urethra to support it, creating a backstop against which the urethra could be compressed, resulting in continence (Kelly HA Dumm WM: Surg Gynecol Obstet 1914:18:444-450). This procedure had the advantage of being relatively simple to perform, and resulted in few complications. Unfortunately, over time research has confirmed that the procedure was not only ineffective, but may in fact result in more

severe stress incontinence than experienced previously. There have been no randomized trials comparing anterior colporrhapy or Kelly plication with suburethral or TVT slings, likely because the anterior repair and Kelly plication fell out of favor for the treatment of SUI prior to the advent of such trials in their current form. A 1997 American Urologic association found that retropubic suspensions were more successful than anterior repairs, though the complication rates were higher. (Leach GE, et al., Female Stress Urinary Incontinence Clinical Guidelines Panel summary report on surgical management of female stress urinary incontinence, J Urol. 1997 Sep;158(3 Pt 1):875-80).

- Needle Suspensions and Retropubic Urethropexies (abdominal/laparoscopic)

Urethropexies, in which the urethra or peri-urethral tissue are supported or "pexed" to ligaments, bone or muscle in the pelvis in an abdominal procedure, were initially described in 1949 by Drs. Marshall, Marchetti, and Krantz (MMK) (The correction of stress incontinence by simple vesicourethral suspension, Xurg Gynecol Obstet 1949;88:509) and modified by JC Burch in 1961 (Urethrovaginal fixation to Cooper's ligament for correction of stress incontinence, cystocele, and prolapse, Am J Obstet Gynecol 1961; 81:281). These procedures were again modified by Drs. Pereyra (A simplified surgical procedure for the correction of stress incontinence in women, West J Surg 1959; 65:223) and Stamey (Endoscopic suspension of the vesical neck for urinary incontinence, Surg Gyencol Obstet 1973; 136:547) to allow for the vaginal (instead of abdominal) placement of sutures, thus making these procedures minimally invasive. These minimally invasive procedures (also called needle suspension procedures) were found to be inferior to abdominal procedures (71% success rate vs. 84% success rate). Needle procedures have not been compared with TVT procedures as they fell out of favor before an adequate literature could be developed. A meta-analysis of 10 trials comparing needle suspension techniques to open Burch colposuspension demonstrated a higher failure rate in the needle suspension group (34% versus 23%; RR 0, 95% CI 1.5–2.7) (Glazener, CM, et al., Anterior vaginal repair for urinary incontinence in women. Cochrane Database Syst. Rev. CD001755 (2001).

Urethropexies, specifically the Burch Urethropexy, have persisted over many years as a useful treatment for stress urinary incontinence. Overall cure rates for the abdominal urethropexy procedures range from 68-88% at one year, and 70% five years after the procedure (Cochrane Database Syst Rev. 2012 Jun 13;(6)). Laparoscopic and abdominal Burch procedures have similar success rates but less operative time, lower complication rates, and shorter hospital stays were seen in patients undergoing laparoscopic Burch (Moehrer B., et al., Laparoscopic colposuspension: a systematic review, BJOG. 2003 Mar;110(3):230-5). The Burch urethropexy appears to be the most durable of the urethropexies (Cochrane Database Syst Rev. 2012 Jun 13;(6) with less incontinence than MMK procedures over 1-5 years (RR0.38; 9%CI 0.18-0.76). Notably, the long-term success of open Burch colposuspension has been demonstrated with an 84% success rate at 7 years in 262 patients (Sivaslioglu AA, et al., (2007) A randomized comparison of transobturator tape and Burch colposuspension in the treatment of female stress urinary incontinence, Int Urogynecol J Pelvic Floor Dysfunct 18(9):1015–1019). However, longer term success rates have declined significantly. Kjolhede followed 190 women who

underwent open Burch colposuspension and significant urinary incontinence was demonstrated in 56% of patients at 14 years, while only 19% of women remained completely dry (Long-term efficacy of Burch colposuspension: a 14-year follow-up study. Acta Obstet Gynecol Scand. 2005 Aug;84(8):767-72).

- Bladder neck slings

The retropubic sling procedure, using a variety of materials for urethral support was first described in 1907. Though there were many different materials used to support the urethra, a common theme was the placement of the sling underneath the bladder neck, where the urethra meets the bladder itself. The technique used in modern pubo-vaginal slings was described by AH Aldridge (Am J Obstet Gynecol 1942; 44:398-411) and later by T Mullin (Retropubic urinary surgery, E&S 1949). This technique formed a sling from rectus fascia. When compared to urethropexy (Cochrane Database Syst Rev. 2011 Jan 19;(1)), patients reported incontinence was less in slings at one year postoperatively, but with a higher risk of postoperative complications, more frequent urinary tract infections, and a longer duration of catheter use.

In the largest multicenter RCT to date comparing rectus fascia pubovaginal slings to Burch (Albo et al. (N Engl J Med. 2007 May 24;356(21):2143-55. Epub 2007 May 21) 655 women were followed for 24 months. Success (defined as no self-reported symptoms of SUI, a negative stress test and no retreatment for SUI) was higher in the pubovaginal sling group than the Burch colposuspension group (66% versus 49%; P <0.001). However, pubovaginal slings were associated with an increased risk of UTI (48% versus 32%; P <0.001), voiding dysfunction (14% versus 2%; P <0.001), and postoperative urge incontinence requiring treatment (27% versus 20%; P = 0.04).

In a follow up report, Brubaker et al (J Urol. 2012 Apr;187(4):1324-30) described the results at 5 years in 482 patients (73.6% of the initial group), and found that continence rates had decreased in both groups. Continence rates were higher in the pubovaginal sling group (30.8%, 95% CI 24.7–36.9) than in the Burch group (24.1%, 95% CI 18.5–29.7; P = 0.002). Patient satisfaction decreased in both groups (from 87% to 83% in the sling group and from 79% to 73% in the Burch group) but remained higher for patients who underwent pubovaginal sling (83% versus 73%; P = 0.03). Adverse events were similar in both groups at 24 months (10% in the Burch colposuspension group and 13% in the pubovaginal sling group; P = 0.2) and at 5 years (10% in the Burch group and 9% in the pubovaginal sling group).

- Bulking Agents

Periurethral bulking agents involve the injection of a material along the urethra, intended to compress the urethra, resulting in continence. These were described using cod liver oil as the injected material in 1938 (Obstet Gyaecol Br EmP 1938;4:67-73). More recently, injected materials include collagen (no longer commercially available), silicone, carbon beads and calcium hydroxylapatite. Cochrane database review concluded there was not evidence to support significant difference among injectables, but that the low risk, low complication procedure could

be useful in certain women. Surgical repairs were more efficacious, though all of these had significantly higher complication rates (Cochrane Database Syst Rev. 2012 Feb 15;(2)).

- Artificial sphincters

Artificial urinary sphincters are inflatable cuffs placed around the urethra. These procedures are infrequently placed in women (67 placed in women in the United States in 2008), and more commonly in women with a diagnosis of neurogenic bladder than for SUI (Matsushita, K, et al., International variation in artificial urinary sphincter use, Urology. 2012 Sep;80(3):667-72).

Mid-urethral slings

Tension-Free vaginal tape (TVT) was first described by Ulmsten and Petros in Sweden in 1995 (Intravaginal slingplasty (IVS): an ambulatory surgical procedure for treatment of female urinary incontinence, Scand J Urol Nephrol. 1995 Mar;29(1):75-82). These slings were different from the previously described pubo-vaginal slings in at least four ways. First, TVT slings were placed at the level of the mid-urethra, instead of the bladder neck. It was placed there based on a theory of continence developed by Ulmsten and Petros called the Integral Theory, which states that urinary incontinence (and other pelvic floor dysfunction) is caused by connective tissue laxity in the vagina or its supporting ligaments (Petros PE (2006)). The sling acts as a back-stop or hammock, compressing the urethra when there is increased intraabdominal pressure generated during physical activity. Second, the procedure involved placement of the sling through the retropubic space using trocars, resulting in a minimally invasive approach that could be accomplished vaginally. Third, the slings were intended to be placed in a tension-free manner, resulting in their engagement only during Valsalva (bearing down). Finally, the synthetic mesh used for these slings was constructed in such a way that no anchoring was required. Instead, the sling was self-retaining, attaching itself along the length of the sling as a property of the mesh construction itself (Rogers, ed Female Pelvic Medicine and Reconstructive Surgery, 2013 ISBN 0-07-175641-8).

- Ethicon and TVT

In 1995, after observing the sling procedure performed by Dr. Ulmsten, Dr. Axel Arnaud negotiated for the device and purchased the rights to the product for Ethicon. In 1996, Petros and Ulmsten reported a series of slings that were initially described as a modification of the intravaginal sling-plasty. In this series they reported that 75 patients underwent the procedure with no significant intraoperative or postoperative complications. No patient had bleeding and no bladder perforations occurred. The operative time was only 22 minutes and all patients left the hospital on the same day. They reported an 84% success rate. In 1998, the TVT sling was introduced in the United States. Since that time it has become one of the most studied and utilized procedures for the treatment of female stress urinary incontinence.

- TVT-O Development

The transobturator approach was introduced in 2001by deLorme (Eur Urol. 2004 Feb;45(2):203-6) with the aim of decreasing further the risks of perioperative bladder, bowel, and vascular complications reported rarely with the retropubic approach. Based on the 'hammock theory' of female SUI (Am J Obstet Gynecol 1994 170:1719), the mesh is placed under the urethra through the obturator membrane and obturator internus muscle in the horizontal plane in order to support the urethra at times of increased intraabdominal pressure, thus preventing leakage.

Transobturator mesh slings can be placed via an outside-in approach or an inside-out approach.

The safety and efficacy of the inside-out TVT-O was investigated by Waltregny et al. (J Urol. 2006 Jun;175(6):2191-5) in a prospective, observational trial that found a subjective and objective cure rate of 91% for 253 women at 12 months' follow-up. Postoperative voiding symptoms were reported in <10% of patients. No bladder or urethral perforations occurred during the procedures, and no vaginal or urethral mesh erosions were noted after surgery. Quality of life was significantly better after surgery than at baseline (P <0.0001). A follow-up study after 3 years revealed similar results (Eur Urol. 2008 Feb;53(2):401-8).

The inside-out and outside-in approaches to the transobturator mid-urethral sling have been compared in several meta-analyses. Most recently, a Cochrane review (Cochrane Database Syst Rev. 2015 Jul 1;(7)) encompassing more than 760 reported similar subjective cure rates between transobturator tapes passed using a medial-to-lateral and a lateral-to-medial approach (RR 1.00, 95% CI 0.96 to 1.06). They also found that voiding dysfunction was more frequent in the medial-to-lateral group (RR 1.74, 95% CI 1.06 to 2.88) but vaginal perforation was less frequent in the medial-to-lateral route (RR 0.25, 95% CI 0.12 to 0.53; 3 trials, 541 women). Latthe (BJU Int. 2010 Jul;106(1):68-76) also found an equal rate of both subjective (OR 1.37, 95% CI 0.93–2.00; P >0.05) and objective success rates (OR 1.06, 95% CI 0.65–1.73; P >0.05). Bladder injury and voiding difficulties were less frequent with the inside-out technique than the outside-in technique (OR 0.17, 95% CI 0.005–0.05 and OR 0.49, 95% CI 0.24–1.04, respectively).

Multiple studies confirm that TVT-O is safe and effective in the long term. These studies include, among many others: Tommaselli GA, Tension-free vaginal tape-obturator and tension-free vaginal tape-Secur for the treatment of stress urinary incontinence: a 5-year follow-up randomized study, Eur J Obstet Gynecol Reprod Biol. 2015 Feb; 185:151-5; Tommaselli GA, Medium-term and long-term outcomes following placement of mid-urethral slings for stress urinary incontinence: a systematic review and metaanalysis, Int Urogynecol J. 2015 May 20; Athanasiou S, Seven years of objective and subjective outcomes of transobturator (TVT-O) vaginal tape: why do tapes fail? Int Urogynecol J. 2014 Feb; 25(2):219-25; Laurikainen E, Five-year results of a randomized trial comparing retropubic and transobturator mid-urethral slings for stress incontinence, Eur Urol. 2014 Jun;65(6):1109-14; Serati M, TVT-O for the treatment of pure urodynamic stress incontinence: efficacy, adverse effects, and prognostic factors at 5-year follow-up, Eur Urol. 2013 May; 63(5):872-8; Cheng D, Tension-free vaginal tape-obturator in the treatment of stress urinary incontinence: a prospective study with five-year follow-up, Eur J

Obstet Gynecol Reprod Biol. 2012 Apr; 161(2):228-31; Liapis A, Efficacy of inside-out transobturator vaginal tape (TVT-O) at 4 years follow up. Eur J Obstet Gynecol Reprod Biol. 2010 Feb; 148(2):199-201.

- TVT Device and placement

The device comes in a box containing the sling, the trocars, and instructions for use. A rigid catheter guide is packaged separately. The procedure is performed with a patient in the lithotomy position. The sling is composed of mesh measuring 1.1 x 40 cm, encased in a plastic sheath designed to maintain sterility and allow the mesh to slide easily through tissue. The long ends of the mesh are swedged on to metal trocars which are used to pass the mesh and plastic sheath through bilateral tunnels in the vaginal mucosa made through a midline vaginal incision approximately 1.5cm in length, at the level of the mid-urethra. Trocars are guided laterally to perforate the endopelvic fascia and are then angled upward behind the pubic bone, perforating the rectus sheath and exiting the skin 2cm lateral to the midline on the abdomen. A cystoscopy is performed to exclude unintentional bladder perforation, and if identified, the trocar is removed and replaced until it is not visible in the bladder. Once placed, the trocars are excised from the mesh, and the plastic sheath is removed in such a way that the mesh is positioned without tension under the mid-urethra. The abdominal ends of the mesh are cut beneath the surface of the skin once placement is complete, and the vaginal incision is closed with a delayed-absorbable suture. The abdominal incisions may be covered with bandages or glue.

- TVT-O Device and placement

The device comes in a box containing the sling, trocars, a winged-guide, and instructions for use. The procedure is performed with a patient in the lithotomy position. The encased in a plastic sheath is swedged onto plastic passers, which are applied with attached to the helical trocars. A vaginal midline incision is created approximately 1.5 cm in length, at the level of the mid-urethra, until the obturator membrane is encountered. A narrow scissors is used to perforate the obturator membrane, and then the winged guide is then used to protect the obturator nerve and blood vessels during trocar placement. The winged guide is placed in the perforation to protect the obturator nerve and vessels during trocar placement. The trocar is rotated around the pubic bone and through the obturator membrane, and then exits the thigh just inferior to the adductor longus tendon at the level of the clitoris bilaterally. A cystoscopy is performed to exclude unintentional bladder perforation, and if identified, the trocar is removed and replaced until it is not visible in the bladder. Once placed, the trocars are excised from the mesh, and the plastic sheath is removed in such a way that the mesh is positioned without tension under the mid-urethra. The lateral ends of the mesh are cut beneath the surface of the skin once placement is complete, and the vaginal incision is closed with a delayed-absorbable suture. The lateral incisions may be covered with bandages or glue.

In contrast, for outside-in approach, the trocar is passed into the inner thigh (a small incision made just inferior to the insertion point of the adductor longus tendon at the level of the clitoral hood) through the obturator membrane and exits through the periurethral dissection.

- Mesh Characteristics

Mesh is commonly used in both general surgery procedures and gynecologic procedures. An effort to identify and/or create an ideal mesh has been ongoing since the 1950's (Iglesia, CB, et al., The use of mesh in gynecologic surgery, Int Urogynecol J Pelvic Floor Dysfunct. 1997;8(2):105-15). An ideal mesh should not induce an untoward inflammatory response, must not be carcinogenic and cause allergy or hypersensitivity. It must resist mechanical stress, be able to be sterilized, and be resistant to infection (Cosson, M., et al., Mechanical properties of synthetic implants used in the repair of prolapse and urinary incontinence in women: which is the ideal material? Int Urogynecol J Pelvic Floor Dysfunct. 2003 Aug;14(3):169-78).

The TVT mesh is a monofilament, knitted, macroporous lightweight polypropylene synthetic mesh. Macroporous, or type I mesh is woven in such a way that the pores, or spaces in between the weave, are greater than 75 microns (Amid PK. Classification of biomaterials and their related complications in abdominal wall hernia surgery. Hernia. 1997;1:15–21)). Like the mesh for TVT, most macroporous meshes are monofiliaments. In contrast to multifilamentous mesh (with pore sizes less than 10 microns), macroporous meshes have greater distances between the filaments. In the case of TVT mesh, the pores are 1379 microns. (Moali, PA, et al., Tensile properties of five commonly used mid-urethral slings relative to the TVT, Int Urogynecol J (2008) 19:655-63). This means that cells within the body such as macrophages, fibroblasts, blood vessels and collagen fibers can fit inside the pores. Type I meshes thus avert infection in the human body in two ways. First, cells that fight infection such as macrophages are able to enter the mesh, deterring the growth of bacteria within the mesh. Second, cells such as fibroblasts and endothelial cells (components of blood vessels) result in rapid fibroplasia and angiogenesis. This also resists infiltration and growth of bacteria (Arnaud, JP, et al., Critical evaluation of prosthetic materials in repair of abdominal wall hernias: new criteria of tolerance and resistance, Am J Surg. 1977 Mar;133(3):338-45). In addition, the plastic sheath covering the sling allows for more sterile mesh placement. Histologic evaluation of mesh after two years has confirmed no evidence of inflammatory response with the TVT mesh (Int Urogynecol J (2001) (Suppl 2):S19–S23).

Mesh that is knitted (like polypropylene) has an advantage over woven mesh (like Merselene), in that knitted weave is flexible, has high tissue conformity, and frays less than woven mesh. In addition, knitted polypropylene used in the TVT has superior elasticity and strength. As such, in vivo it has not been found to contract or change position once it has been implanted, and although scar tissue is expected to form at the site of any surgery, the scar tissue formed during the placement of TVT does not result in contraction of the mesh or changes in the function or motion of the urethra over time (Lukacz ES, et al., The effects of the tension-free vaginal tape on proximal urethral position: a prospective, longitudinal evaluation, Int Urogynecol J Pelvic Floor Dysfunct. 2003 Aug;14(3):179-84; Nilsson, C.G., Palva, K., Aarnio, R. et al., Seventeen years' follow-up of the tension-free vaginal tape procedure for female stress urinary incontinence, Int Urogynecol J (2013) 24: 1265). Despite multiple systemtic reviews evaluating complications of slings, I am not aware of literature finds that mesh contraction is associated with TVT (Ford AA,

Rogerson L, Cody JD, Ogah J. Mid-urethral sling operations for stress urinary incontinence in women. Cochrane Database Syst Rev. 2015 Jul 1;7:CD006375. PMID: 26130017 (2015)).

The TVT polypropylene mesh is not carcinogenic. King et al (Is there an association between polypropylene mid-urethral slings and malignancy? Urology. 2014 Oct;84(4):789-92) reviewed 2361 patients who had undergone TVT. The bladder cancer occurred in 1 patient and vaginal cancer in 1 patient. This is the same rate as is found in the general population (i.e. people who have not had TVT slings). In addition, there were no sarcomas (muscle cancers) identified. Similarly, Linder et al. found only 2 cases amongst 2,474 who underwent polypropylene MUS placement (0.08%) with a mean follow up of 61.5 months (Evaluation of the local carcinogenic potential of mesh used in the treatment of female stress urinary incontinence. Int Urogynecol J. 2016 Feb 10. doi: 10.1007/s00192-016-2961-4). In this study, 49 cancer diagnoses occurred before the date of sling placement. Thus, the background rate of cancer in these patients was 2% (49 out of 2,474). There are no case reports in the medical literature identifying cancers caused by or associated with TVT mesh. AUGS/SUFU addresses this issue, stating:

> *There is no compelling evidence supporting human malignant transformation related to* ***polypropylene despite the millions of individuals implanted with various forms of this material*** *span well over a half century world-wide.* (AUGS-SUFU FAQs by Patients on Mid-urethral Slings for SUI March 2014).

Moali (Tensile properties of five commonly used mid-urethral slings relative to the TVT, Int Urogynecol J (2008) 19:655-63) evaluated the tensile properties of TVT (Ethicon/Gynecare) mesh compared to the meshes of other commercially available slings. Their findings identified a unique tensile behavior of the Ethicon mesh, which was characterized by an initial low stiffness behavior that results in easy elongation with minimal force. With increasing force, there is higher stiffness. The mesh can be permanently elongated by more than 10% of the original length. The authors suggest that this is likely the reason for the low erosion rates and bladder obstruction rates seen in TVT.

Laser vs. Mechanical Cut Mesh

The original slings marketed in the US were mechanically cut, and thus the majority of the research performed and the clinical trials in the literature report about such slings. Over 1000 trials and studies have reported the clinical effectiveness of such slings, and there has been no report of any intrinsic defect. In 2007, Ethicon changed from mechanically cut slings to laser cut slings, though the mechanically cut slings remain available. Review of the internal Ethicon documents reporting on engineering evaluation of sling properties did not identify differences in the physical characteristics of laser cut vs. mechanically cut slings. Additionally, laser cut slings have not been shown to increase the risk of mesh erosion or exposure (Neuman M, Transobturator vs single-incision suburethral mini-slings for treatment of female stress urinary incontinence: early postoperative pain and 3-year follow-up, J Minim Invasive Gynecol. 2011 Nov-Dec;18(6):769-73)

Fraying and particle loss

Fraying of mechanically cut slings can occur when the sling is under a high degree of stress tension. These conditions are not encountered in vivo when physiologic stress is the type of stress exposure. TVT and TVT-O, when placed properly are placed in a tension free manner. Stretching of the sling should not occur if the sling is placed correctly. When used under normal conditions with normal placement technique, curling or fraying of the edges of the sling does not occur.

There has been a concern raised that mechanically cut mesh may fray and that this could lead to pain or erosion due to the presence of mesh particles. In my review of the literature, I was unable to identify scientific support for this concern. There have been no studies identifying particle loss as a cause of complications in TVT/TVT-O. Prolene is the material used in mesh, and prolene sutures have been used in surgery for many decades. If theoretic fraying and release of particles occurs, the particles would be composed of this same prolene which has been used safely for years. In addition, fraying is caused by undue stress placed on mesh, which as mentioned above is not an issue when the mesh is placed using proper technique. Photographs that involve a roped, frayed portion of mesh are examples of what can happen to mesh when a supra-physiologic stress is placed on it. The mesh used in TVT/TVT-O is not subject to such stress during normal placement, nor once in vivo. The theory that particles from mechanically cut TVT lead to adverse clinical effects is not supported by the medical literature or my clinical experience.

Cytotoxicity and Degradation

Prolene mesh is not cytotoxic. Evaluation of implanted mesh has confirmed tissue ingrowth and a lack of inflammation. If the mesh were cytotoxic, one would expect the opposite, including tissue necrosis, mesh rejection, and failed incorporation of mesh by the surrounding tissues. This is not consistent with clinical studies showing excellent safety, tolerability, low levels of infection, and mesh erosion, and efficacy. In addition, polypropylene mesh appears to remain effective over time, which suggests that degredation of the mesh does not occur. Clave (Int Urogynecol J. 2010 Mar;21(3):261-70) reported cracking of the surface of polypropylene mesh evaluated after explantation from patients. However, the mechanical properties of mesh and the possible damage to the mesh during its removal could not be evaluated. Given the excellent medium and long term results from slings (Ford et al., Cochrane Database Syst Rev. 2015 Jul 1;(7)), there is no evidence that the findings of Clave correspond to functional compromise. Finally, guidance from specialty societies point out that these concerns are not supported by extensive peer reviewed literature related to polypropylene mesh repair (AUGS-SUFU FAQs by Providers on Mid-urethral Slings for SUI March 2014). My own review of the literature and clinical experience has brought me to the conclusion that the degredation of polypropylene mesh probably does not occur, but even if it does, there is no clinically significant impact. To date, polypropylene is the best available material for slings, and has been studied more than any other material used for this purpose.

Prolene mesh does not cause chronic inflammation or infection. Metaanalyses as mentioned above confirm that infection in sling placement is very rare. It is further difficult to differentiate

infection at the surgical site (which is a known complication of all surgical procedures) from that which is due to the mesh. I have personally implanted hundreds of TVT/TVT-O and have never seen an infection

Mesh erosion

Erosion, or exposure of mesh in the vagina, bladder and urethra are a common and well-known concern. Although commonly asymptomatic, mesh erosions can be symptomatic by causing increased vaginal discharge or painful sexual intercourse in the male partner. Management of mesh erosion can be done with the application of vaginal estrogen to stimulate tissue growth of the vaginal tissue over the mesh, or by excision of the mesh in the office or operating room.

The rate of mesh erosions from TVT slings using polypropylene mesh is very low (around 1-3%), and surgical excision is uncommon. In a Cochrane systematic review evaluating 4743 patients, the vaginal mesh erosion rate was 2.09% (Cochrane Database Syst Rev. 2015 Jul 1). A population-based cohort identified a mesh erosion rate requiring surgical revision of 2.5% over 9 years. This evaluation looked at over 188,000 women who underwent sling placement (Jonsson, F., et al., Sling revision/removal for mesh erosion and urinary retention: long-term risk and predictors, Am J Obstet Gynecol. 2013 Jan;208(1):73.e1-7). An additional population based review reported a mesh removal rate of 2.2% (Welk, B, et al., Removal or Revision of Vaginal Mesh Used for the Treatment of Stress Urinary Incontinence, JAMA Surg. 2015 Dec;150(12):1167-75). Tamussino (Am J Obstet Gynecol. 2007 Dec;197(6):634.e1-5) summarized the findings of the Austrian registry of 2795 patients who underwent transobturator retropubic sling with and without concomitant prolapse repair. Only 0.7% underwent repeat operation for mesh erosion. Patient factors may modify the risk of mesh erosion. Increasing age, diabetes mellitus, current smoking, vaginal incision > 2cm, a repeat vaginal incision made after the original surgery, and previous surgery for incontinence or pelvic organ prolapse placed patients at increased risk of mesh erosion (Kokanali, MK, et al., Risk factors for mesh erosion after vaginal sling procedures for urinary incontinence, Eur J Obstet Gynecol Reprod Biol. 2014 Jun;177:146-50). However, not all studies have identified these risk factors (Unger CA, et al., Indications and risk factors for mid-urethral sling revision, Int Urogynecol J. 2016 Jan;27(1):117-22), so there is not yet consensus.

- Efficacy

The TVT as described by Ulmsten and Petros, and released into the United States by Ethicon, has the longest studies available demonstrating efficacy, and multiple reports comparing it to other procedures (as mentioned above) used to treat stress urinary incontinence.

As the procedure was initially developed and performed in Nordic countries with developed patient registries, there is a cohort of women who underwent the procedure when it was initially developed who have been followed for over 17 years (Nilsson, C.G., Palva, K., Aarnio, R. et al., Seventeen years' follow-up of the tension-free vaginal tape procedure for female stress urinary incontinence, Int Urogynecol J (2013) 24: 1265). At last report, 78% of women, all with stress incontinence alone, who initially underwent TVT placement were available for follow up. Of note, the sling used for on these patients was "identical to the presently available" TVT except

that the trocars used were 6mm instead of 5mm. This report identified a cure rate of 87.2% after 17 years. In this study Nilsson observes the following:

- *There seems to be no shrinkage of the TVT mesh over time, as suggested by postvoid residual volumes within normal ranges, except for 2 patients with concomitant diseases (Parkinson's, grade III cystocele).*

- *The mesh complications seen in association with urogenital prolapse surgery that have alerted the FDA might not be caused by the mesh material itself. As long as a type I material is used the complications could be the result of improper training of the surgeon, resulting in an inappropriate surgical technique or choosing the wrong indication or wrong patient for the graft procedure.*

- *The present report suggests that using a type I, macroporous, monofilament, lightweight, and soft polypropylene mesh, the risk of mesh complications even 17 years after implantation under the vaginal mucosa is negligible provided the surgery is performed by a trained and experienced surgeon.*

A recent Cochrane review identified an average 5-year subjective cure rate of 84.3% (range 51-88%) in four trials involving a total of 714 women, which is consistent with the results of the initial cohort. Long-term objective cure rates in this same review were noted to be 87.2%.

Efficacy of the TVT has been established when compared to multiple other procedures for the treatment of urinary incontinence and the preponderance of literature allows for pooling of data in systematic reviews to appropriately integrate and interpret the many studies.

- Open retropubic colposuspension was found to have equivalent rates of incontinence when compared to slings within one year of treatment (Cochrane Database Syst Rev. 2016 Feb 15;2). A systematic review in 2010 (Novara G, et al., Updated systematic review and meta-analysis of the comparative data on colposuspensions, pubovaginal slings, and mid-urethral tapes in the surgical treatment of female stress urinary incontinence, Eur Urol. 2010 Aug;58(2) found that in 39 randomized controlled trials, patients had significantly higher overall cure rates with TVT than with Burch culposuspension.

- A systematic review comparison of TVT to needle suspension was attempted, but there were not enough good quality studies available to provide a comparison. However, there is data confirming that needle suspensions have inferior success rates when compared to retropubic colposuspensions when evaluated within one year of surgery (Cochrane Database Syst Rev. 2014 Dec 17;(12)).

- When compared with traditional sling operations, a Cochrane review of twelve trials identified equal effectiveness in the first year. More recently, Schimpf et al (Sling surgery for stress urinary incontinence in women: a systematic review and metaanalysis, Am J Obstet Gynecol. 2014 Jul;211(1):71.e1-71) found in a systematic

review that subjective cure rates in mid-urethral slings were higher than traditional slings.

- Risks

As with all surgical procedures there are risks to the TVT procedure. Complications that are common and well-known to pelvic floor surgical procedures, specifically procedures to treat stress urinary incontinence, include bleeding, infection, pain, dyspareunia, damage to surrounding organs such as nerves, blood vessels, tissue, and organs such as the bladder, the urethra, and the vagina. There are also complications that occur in most procedures to treat stress urinary incontinence and include urinary retention and voiding dysfunction such as urgency incontinence, urinary urgency or frequency. Reoperation and failure of the surgery to correct the problem are also known complications of surgical procedures including the TVT sling. Finally, there are complications due to unique aspects of the TVT itself, primarily those resulting from the use of mesh. Mesh related complications were discussed previously. There is an abundance of literature characterizing these risks for the TVT.

The safety of retropubic and transobturator mid-urethral slings has been established and compared with other surgical treatments of stress urinary incontinence.

- The 2015 Cochrane Review concluded that "*midurethral sling operations are the most extensively researched surgical treatment for stress incontinence in women, have a good safety profile.... and are highly effective in the short and medium term... accruing evidence demonstrates their effectiveness in the long term.*" The authors also concluded that mid-urethral slings have a "*positive impact on improving quality of life of women with stress incontinence.*"

- Ford et al. evaluated complication rates from large national registries including the MAUDE database. They identified the following complication rates for the retropubic mid-urethral sling: bladder perforation 2.7 – 3.9%, reoperation rates relating to tape insertion or postoperative voiding dysfunction 1.6% - 2.4%, urinary retention rate was 1.6%, pelvic hematoma 0.7% - 1.9%, infection rate was 0.7%, vaginal tape erosion/extrusion rate was 1.5%, groin pain occurred in 0.4% of women. These rates were similar to those reported among the 12,113 patients included in the randomized controlled trials evaluated in the review. Similar complications were reported for transobturator slings: bladder perforation 0.4%, reoperation rates relating to tape insertion 0.8% - 2.2%, urinary retention 0.5%, pelvic hematoma 0.5%, infection rate 0.6%, vaginal tape erosion/extrusion rate was 0.4%, and groin pain occurred in 1.6% of women. (Mid-urethral sling operations for stress urinary incontinence in women. Cochrane Database Syst Rev. 2015 Jul 1).

- Retropubic slings compared with open colposuspension were equally safe when comparing complication rates between the two procedures in a recent Cochrane review (Cochrane Database Syst Rev. 2016 Feb 15;2). Women undergoing Burch

colposuspension were twice as likely to develop new or recurrent pelvic organ prolapse when compared to those undergoing sling procedures. Ward et al (Prospective multicenter randomized trial of tension-free vaginal tape and colposuspension as primary treatment for stress incontinence, BMJ. 2002 Jul 13;325(7355):67) found that TVT slings had a higher risk of bladder perforation than colposuspension, but lower postoperative complications like delayed resumption of voiding. Novara described more frequent bladder perforation in TVT procedures, but risk of pelvic hematoma, urinary tract infections, urinary urgency and urgency incontinence, urinary retention and reoperation were the same between the two procedures Eur Urol. 2010 Aug;58(2):218-38.

- There was not data available to directly compare the safety of bladder neck needle suspension with TVT sling.

- Minimally invasive synthetic slings had less de novo detrusor activity such as urinary urgency, frequency and urgency incontinence than traditional sling operations, and a lower risk of complications overall when compared to traditional bladder neck slings (Cochrane Database Syst Rev. 2011 Jan 19;(1)). Less blood loss, transfusion, and wound infections were found in patients undergoing TVT slings (Schimpf, et al., Sling surgery for stress urinary incontinence in women: a systematic review and metaanalysis, Am J Obstet Gynecol. 2014 Jul;211(1):71.e1-71). Novara reported significantly lower rate of bladder perforation in traditional slings, a similar, low rate of pelvic hematoma in both groups, and a lower risk of urinary retention, and reoperation in patients undergoing TVT (Eur Urol. 2010 Aug;58(2):218-38). Ogah et al (Cochrane Database Syst Rev. 2009 Oct 7;(4)) performed a meta-analysis of 62 trials involving 7,101 patients and evaluated the short-term clinical effects of minimally invasive synthetic mid-urethral sling procedures for the treatment of SUI. Eight RCTs (599 patients) compared synthetic mid-urethral slings with pubovaginal slings, and the overall subjective cure rate within 12 months was similar between the two (73% vs 71%, RR 1.03, 95% CI 0.94–1.13). However, the mid-urethral slings were associated with shorter operative times, quicker recovery, and fewer postoperative complications. Rates of new onset urgency and urgency incontinence were lower after mid-urethral sling compared to bladder neck slings

The quality of life impact of retropubic mid-urethral slings has been evaluated and compared with other surgical treatments of stress urinary incontinence.

- There was no difference in quality of life scores from trials comparing open retropubic colposuspension to suburethral sling, except that the colposuspension group had less improvement in emotional and social functioning, vitality and mental health six months and two years after the procedure, as identified on the quality of life short-form-36 (Cochrane Database Syst Rev. 2016 Feb 15;2).
- There was not available data directly comparing the quality of life impact of needle suspension procedures to TVT (Cochrane Database Syst Rev. 2014 Dec 17;(12).
- There was no difference in quality of life scores on validated (6 studies) and non-validated (2 studies) questionnaires when comparing TVT to traditional retropubic slings.

In addition, there was less need for pain medication, and patients (Cochrane Database Syst Rev. 2011 Jan 19;(1)).

The effects of retropubic mid-urethral slings on sexual function has been evaluated and compared with other surgical treatments of stress urinary incontinence

- Pain and sexual dysfunction are higher with Burch urethropexy and autologous pubovaginal sling than mid-urethral sling The American Urologic Association (AUA) 2012
- There were not available data to directly compare sexual function outcomes between needle suspension procedures and TVT.
- Dyspareunia increases when combined with vaginal prolapse surgery. (Siddighi S, Hardesty JS. Urogynecology & Female Pelvic Reconstructive Surgery. ISBN 0-07-144799-7.)
- Patients undergoing both retropubic and transobturator midurethral slings were found to have improved sexual function after their procedures, including fewer complaints of pain with sex, fear of leakage with sex, and actual leakage during sexual intercourse (Zyczynski HM, et al. Sexual activity and function in women more than 2 years after mid-urethral sling placement. Am J Obstet Gynecol. 2012 Nov;207(5):421.e1– 6.).

The economic impact and operative characteristics of retropubic mid-urethral slings has been evaluated and compared with other surgical treatments of stress urinary incontinence

- Patients undergoing TVT are able to go home sooner from the hospital, and return to work and exercise sooner than those undergoing Burch retropubic urethropexy (Ward, et al., Prospective multicenter randomised trial of tension-free vaginal tape and colposuspension as primary treatment for stress incontinence, BMJ. 2002 Jul 13;325(7355):67).

- There was not available data directly comparing the economic impact and operative statistics of needle suspension procedures to TVT (Cochrane Database Syst Rev. 2014 Dec 17;(12).

- A randomized trial comparing TVT to traditional sling reported shorter operating times, less overall cost (Kondo, A., et al., Efficacy, safety and hospital costs of tension-free vaginal tape and pubovaginal sling in the surgical treatment of stress incontinence. J Obstet Gynaecol Res. 2006 Dec;32(6):539-44). This was confirmed by the results of a systematic review that identified shorter lengths of surgery and decreased length of stay compared to pubovaginal slings (Schimpf, et al., Sling surgery for stress urinary incontinence in women: a systematic review and metaanalysis, Am J Obstet Gynecol. 2014 Jul;211(1):71.e1-71).

Pain resulting from of mid-urethral slings, both retropubic and obturator approaches, has been evaluated.

- Groin Pain

Pain in the groin or thigh is a complication of mid-urethral slings that occurs more commonly with the transobturator approach than retropubic surgery. Ford et al (Cochrane Database Syst Rev. 2015 Jul 1;(7)) found that studies including 3221 women there was a significantly higher rate of groin pain in those undergoing transobturator sling than those undergoing retropubic sling.(6.4% vs. 1.3% RR 4.12 95%CI 2.71-6.27). However, the pain was short in duration (duration ranged from 2-52 weeks, Mean 8 weeks). In a trial not included in this analysis, Laurikainen described 16% (21/131) of women experienced pain in the obturator group compared to 1.5% (2/136) in the retropubic sling group. All pain was resolved within 2 months, with most resolving by 2 weeks. (Five-year results of a randomized trial comparing retropubic and transobturator mid-urethral slings for stress incontinence. Eur Urol 65:1109–1114) In meta-analyses, Long et al. and Latthe et al. confirmed that groin or thigh pain was reported more frequently after transobturator insertion than retropubic procedures. (Comparison of tension-free vaginal tape and transobturator tape procedure for the treatment of stress urinary incontinence. Curr Opin Obstet Gynecol 2009;21:342-7). In reviews that added additional studies, Latthe et al. confirmed that groin or thigh pain was reported more frequently after transobturator insertion than retropubic procedures (BJU Int. 106, 68–76 (2010)).

In multiple long-term follow up reports, the groin pain was found to have resolved completely. Athanasiou et al. found that no patients reported persistent groin pain at the long-term follow-up. (Seven years of objective and subjective outcomes of transobturator (TVT-O) vaginal tape: why do tapes fail. Int Urogynecol J 2014;25:219–25) Ford et al (Cochrane Database Syst Rev. 2015 Jul 1;(7)

In the most recent and comprehensive systematic review of the literature evaluating the safety of mid-urethral slings (Ford et al., Cochrane Database Syst Rev. 2015 Jul 1;(7)) no difference was found in the overall safety of both transobturator and midurethral slings in trials where overall perioperative complication rates were re-ported there were no statistically significant differences in the rate of perioperative complications (RR 0.91, 95% CI 0.73 to 1.14). This included the rate of mesh erosion was rare and not significantly different between retropubic and transobturator slings (21/1000 (retroupbic) vs 24/1000 (obturator) (RR1.13, 95% CI 3.36-23.00). The authors concluded:

> *Midurethral sling operations have been the most extensively researched surgical treatment for stress urinary incontinence in women and have a good safety profile. Irrespective of the routes traversed, they are highly effective in the short and medium term and accruing evidence demonstrates their effectiveness in the long term.*

- Utilization

TVT slings have become the most common treatment for stress urinary incontinence in women, and it has been called the gold standard for treatment (Nilsson, CG, Creating a gold standard surgical procedure: the development and implementation of TVT, Int Urogynecol J. 2015 Apr;26(4):467-9). One survey found that synthetic mesh slings were used by >99% of the membership of the American Urogynecologic Society (Clemons et al, Female Pelvic Med. & Recon. Surgery, Vol. 19, No. 4, 2013). Many societies and organizations have endorsed this sling as a first line treatment for SUI. Some of these statements include:

American College of Obstetrics and Gynecology/American Urogynecologic Association Practice Bulletin No. 155

- Synthetic midurethral slings demonstrate efficacy that is similar to traditional suburethral fascial slings, open colposuspension, and laparoscopic colposuspension. Compared with suburethral fascial slings, fewer adverse events have been reported with synthetic midurethral slings. Voiding dysfunction is more common with open colposuspension than with synthetic midurethral slings. (Level A evidence)

- There is substantial safety and efficacy data that support the role of synthetic mesh midurethral slings as a primary surgical treatment option for stress urinary incontinence in women. (Level A evidence)

American Urogynecologic Society and Society of Urodynamics, Female Pelvic Medicine and Urogenital Reconstruction Position Statement on Mesh Midurethral Slings for Stress Urinary incontinence, January 3 2014, updated June 2016. Endorsed by American Association of Gynecologic Laparoscopists, American College of Obstetrics and Gynecology, the National Association for Continence, and the Society of Gynecologic Surgeons.

- The polypropylene mesh midurethral sling is the recognized worldwide standard of care for the surgical treatment of stress urinary incontinence. The procedure is safe, effective, and has improved the quality of life for millions of women.

- ***Polypropylene material is safe and effective as a surgical implant.*** Polypropylene material has been used in most surgical specialties (including general surgery, cardiovascular surgery, transplant surgery, ophthalmology, otolaryngology, gynecology, and urology) for over five decades, in millions of patients in the US and the world (personal communication with manufacturers of polypropylene suture and mesh). As an isolated thread, polypropylene is a widely used and durable suture material employed in a broad range of sizes and applications. As a knitted material, polypropylene mesh is the consensus graft material for augmenting hernia repairs in a number of areas in the human body and has significantly and favorably impacted the field of hernia surgery. As a knitted implant for the surgical treatment of SUI, macroporous, monofilament, light weight polypropylene has demonstrated long term durability, safety, and efficacy up to 17 years.

- ***The monofilament polypropylene mesh MUS is the most extensively studied anti-incontinence procedure in history.*** There are greater than 2,000 publications in the scientific literature describing the MUS in the treatment of SUI. These studies include the highest level of scientific evidence in the peer reviewed scientific literature. …..Among historical SUI procedures, the MUS has been studied as long in follow-up after implantation as any other procedure and has demonstrated superior safety and efficacy. No other surgical treatment for SUI before or since has been subject to such extensive investigation.

- ***Polypropylene mesh midurethral slings are a standard of care for the surgical treatment of SUI and represent a great advance in the treatment of this condition for our patients.*** Since the publication of numerous level one randomized comparative trials, the MUS has become the most common surgical procedure for the treatment of SUI in the US and the developed world. This procedure has essentially replaced open and transvaginal suspension surgeries for uncomplicated SUI. There have been over 100 surgical procedures developed for the management of SUI and there is now adequate evidence that the MUS is associated with less pain, shorter hospitalization, faster return to usual activities, and reduced costs as compared to historic options that have been used to treat SUI over the past century. Full-length midurethral slings, both retropubic and transobturator, have been extensively studied, are safe and effective relative to other treatment options and remain a leading treatment option and current gold standard for stress incontinence surgery. Over 3 million MUS have been placed worldwide and a recent survey indicates that these procedures are used by > 99% of AUGS members.

International Urogynecologic Association Position Statement on Mid-Urethral Slings for Stress Urinary Incontinence

- There is robust evidence to support the use of MUS from over 2,000 publications making this treatment the most extensively reviewed and evaluated procedure for female stress urinary incontinence now in use. These scientific publications studied all types of patients, including those with co-morbidities such as prolapse, obesity and other types of bladder dysfunction. It is, however, acknowledged that any operation can cause complications. For MUS these include bleeding, damage to the bladder and bowel, voiding difficulty, tape exposure and pelvic pain; all of these may require repeat surgery but this is uncommon. Nevertheless, the results of a recent large multi-centre trial have confirmed excellent outcomes and a low rate of complications to be expected after treatment with MUS. Additionally, long term effectiveness of up to 80% has been demonstrated in studies including one which has followed up a small group of patients for 17 years.

- As a result, IUGA supports the use of monofilament polypropylene mid-urethral slings for the surgical treatment of female stress urinary incontinence.

American Urologic Association Position statement on the use of vaginal mesh for the surgical treatment of stress urinary incontinence. Revised October 2013

- Suburethral synthetic polypropylene mesh sling placement is the most common surgery currently performed for SUI. Extensive data exist to support the use of synthetic polypropylene mesh suburethral slings for the treatment of female SUI, with minimal morbidity compared with alternative surgeries. Advantages include shorter operative time/anesthetic need, reduced surgical pain, reduced hospitalization, and reduced voiding dysfunction. Mesh-related complications can occur following polypropylene sling placement, but the rate of these complications is acceptably low. Furthermore, it is important to recognize that many sling-related complications are not unique to mesh surgeries and are known to occur with non-mesh sling procedures as well. It is the AUA's opinion that any restriction of the use of synthetic polypropylene mesh suburethral slings would be a disservice to women who choose surgical correction of SUI.

The Royal Australian and New Zealand College of Obstetricians and Gynaecologists Position statement on midurethral slings (March 2014)

- This position statement by the Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) and the Urogynaecological Society of Australasia (UGSA) supports the use of mid-urethral slings (MUS) in the surgical management of female stress urinary incontinence (SUI). This is the type of urinary leakage associated with physical exertion, such as coughing, laughing and sneezing.

- Stress urinary incontinence is an extremely common, burdensome and costly condition for women in Australasia, with a negative impact on a women's quality of life.... Mid-urethral slings are minimally invasive procedures developed in the early 1990s to treat female stress urinary incontinence. These slings are narrow, synthetic polypropylene tapes that are surgically placed beneath the middle part of the urethra (water pipe) to provide dynamic support to stop leakage from the bladder. They have been shown to be as effective as more invasive traditional surgery with major advantages of shorter operating and admission times, and quicker return to normal activities, together with lower rates of complications. This has resulted in MUS becoming the operation of choice in Europe, the United Kingdom, Australasia and the USA for treatment of SUI.

International Continence Society Fact Sheet (July 2013)

- Definitive therapy for SUI is surgical and involves restoring urethral support through use of a sling. Worldwide, midurethral slings comprised of synthetic mesh have become the treatment of choice for SUI. Long-term data are robust and demonstrate durable efficacy with a very low complication rate, particularly in experienced hands.

FDA Considerations about Surgical Mesh for SUI (March 27, 2013)

- Mesh sling procedures are currently the most common type of surgery performed to correct SUI. Based on industry estimates, there were approximately 250,000 of these

procedures performed in 2010.

- The safety and effectiveness of multi-incision slings is well-established in clinical trials that followed patients for up to one-year. Longer follow-up data is available in the literature, but there are fewer of these long-term studies compared to studies with one-year follow-up.

I agree with the above professional society statements as they are consistent not just with my clinical experience, but my extensive review of the medical literature. These guidelines and position statements inform surgeons on the standard of care, the usefulness, utility, desirability of the TVT/TVT-O as well as its safety and do not support the idea that TVT/TVT-O is unreasonably dangerous for its intended use.

Instructions for Use

Ethicon, in compliance with FDA requirements, has developed Instructions for use (IFU), included with each sling. Based on guidance from the FDA (FDA Device Labeling Guidance #G91-1), these instructions include:

- Description of the product
- Indications for use: "…as a pubourethral sling for treatment of Stress Urinary Incontinence (SUI), for female urinary incontinence resulting from urethral hypermobility and/or intrinsic sphincter deficiency."
- Instructions for use
- Contraindications
- Warnings and precautions
- Adverse reactions
- Instructions for cleaning and sterilization

The *GYNECARE TVT*™ Device is a prescription device, which is defined as:

> *A prescription device is, by definition under 21 CFR 801.109, a device which, because of any potentiality for harmful effect, or the method of its use, or the collateral measures necessary to its use, is not safe except under the supervision of a practitioner licensed by law to direct the use of the device, and hence for which "adequate directions for use" (21 CFR 801.5) cannot be prepared* (FDA Device Labeling Guidance #G91-1).

The TVT IFU describes the intended users as "*physicians trained in the surgical treatment of Stress Urinary Incontinence and specifically in implanting the GYNECARE TVT™ Device (GYNECARE TVT*™ Tension-free Vaginal Tape System-Instructions for Use)."

The IFU may be used by a surgeon to familiarize herself with a specific device, including the recommended indications, effects, routes, methods, frequency of use, hazards, contraindications, side effects, and precautions that will guide safe and effective use of the intended device. The purpose of the IFU is thus not intended to provide a surgical education and is not intended to provide comprehensive information regarding details of the diagnosis and treatment of stress

urinary incontinence, patient selection for surgery, pelvic anatomy, surgical technique such as knot-tying or instrument handling, patient positioning, sterile technique, the diagnosis and management of surgical complications, and postoperative care.

Instead, surgeons using the TVT system should possess a background of surgical training resulting in a broad knowledge of all of these topics and many others. Education in these areas are derived from years of training including medical school, many years of residency training, review of published medical literature, and possibly fellowship training.

- The ACGME Program requirements for Graduate Medical Education in Female Pelvic Medicine and Reconstructive Surgery Pt IV.A.5.b)(2)(c) states that "fellows completing the F2 year must demonstrate competence in their knowledge of indications, contraindications, limitations, complications, techniques, and interpretation of results of screening, diagnostic, and therapeutic procedures including surgery for pelvic organ prolapse and urinary incontinence"
- American Urogynecologic Association resident learning objectives "Know the various approaches, both nonsurgical and surgical, for the treatment of urodynamic stress incontinence. Understand the difference between traditional and minimally invasive surgical approaches, e.g. open Burch versus laparoscopic Burch, and traditional pubovaginal sling versus mid-urethral sling.... demonstrate an understanding of the normal anatomy, anatomic interrelationships and variations of the bony pelvis, pelvic girdle and pelvic floor musculature, nerve supply, vasculature, lymphatic drainage, connective tissue supports and the pelvic viscera including the bladder, ureters, urethra, vagina, uterus, rectum, sigmoid colon, small bowel surrounding structures."
- The International Urogynecologic Association (IUGA) has established similar standards for international trainees in FPMRS: "The trainee should receive experience in the theory, practice, and performance of procedures... Minimally invasive slings"

In addition, physicians who have completed training must participate in continuing medical education as a basis for continued medical licensing and certification. Physicians attend conferences, training courses, review current medical literature and may undergo surgical proctoring by experts as they learn and refine their ability to treat specific medical conditions and perform specific surgical procedures.

Pelvic surgeons are thus trained in an ongoing basis to understand the risks, both common and rare, of the surgeries they perform. Retropubic and transobturator mid-urethral sling using polypropylene mesh have known risks. Most of these risks are common to all surgeries for stress urinary incontinence other pelvic procedures that do not use mesh. Examples of this include, but are not limited to, de novo or worsening urgency urinary incontinence, pain, dyspareunia, retention/voiding difficulty, failure of the procedure to effectively treat incontinence, nerve/vessel injury, scarring, wound complications, bleeding, damage to adjacent organs and need for reoperation. These complications may be mild or severe, but all occur to varying degrees and can range from transient to long term concerns in all incontinence surgeries. The instructions for use (IFU) warn of risks of complications in TVT/TVT-O including infection, inflammation, obstruction/retention, fistula formation, mesh erosion and extrusion. It is incumbent upon surgeons to understand the risks of the procedures they perform, including the

risks of the instruments used in the surgery, and the risks of any implants such as polypropylene mesh. The FDA Document 21 C.F.R. 801.109(c), states that risk information for devices used by licensed professionals may be omitted from product labeling if "the article is a device for which directions, hazards, warnings, and other information are commonly known to practitioners licensed by law to use the device." This regulation supports my opinions expressed above.

Ethicon Training

To facilitate safety in procedures involving TVT/TVT-O slings, Ethicon offered training programs in placement of TVT slings, beginning in 1999. This provided an opportunity for those who had already completed residency or fellowship training to learn new techniques that were not available during their training. Phyisician training offered by Ethicon is intended to supplement the surgeon's training and knowledge, and is not a primary source of expertise. Other procedures such as Urethropexy or pubovaginal slings do not have IFU's as a supplemental source of education because they do not exist for these procedures

These programs typically include didactic lectures, videos, hands-on cadaver labs, and an opportunity to "practice" the steps of the procedure on cadavers and on plastic pelvic models. Preceptors at these events include academic and private practice physicians with substantial experience and expertise in pelvic anatomy, pelvic surgery, and TVT sling placement using Ethicon products. The lecture component of the program offers a discussion of patient selection for surgery, contraindications to surgery, tips on avoidance of intraoperative and postoperative complications, and safety. Webinars and telesurgery are also utilized as methods for continuing education and to provide updates about slings.

Surgeons must undergo a credentialing process before being granted privileges to perform procedures at a specific hospital. The requirements for credentialing vary by institution, but may include confirmation of residency and fellowship training, board certification, medical licensure, a review of medical malpractice history and initial proctoring of new physicians. While medical device companies like Ethicon can provide high quality training regarding a specific procedure, it is the individual hospital or medical system that grants and maintains credentialing. Typical credentialing does not grant privileges for a specific product such as TVT/TVT-O or TVT Exact/Abbrevo, but instead privileges for categories such as "treatment of stress urinary incontinence."

Design of TVT and TVT-O

The TVT and TVT-O slings stand in contrast to previously accepted procedures. This includes procedures that now have historical importance such anterior colporrhaphy, Kelly plication, and needle suspensions, all of which have fallen out of favor because they were not as effective as more modern procedures.

Procedures such as Burch urethropexies and pubovaginal slings continue to occupy a place in the armamentarium of a physician who specializes in the treatment of stress urinary incontinence.

However, both of these procedures can pose significant challenges for patients. Abdominal Burch procedures require an abdominal incision and a retropubic dissection, which results in an increased amount of time for recovery from surgery, and may result in increased blood loss and immediate postoperative pain. Laparoscopic Burch procedures may not be as effective as abdominal Burch. Both procedures have less subjective success then TVT. Pubovaginal slings have an increased risk of bleeding, and require a more extensive dissection and in many cases an abdominal incision. This, in addition to the requirement of fascial harvesting may make recovery from surgery longer and more difficult.

The TVT slings addressed many of these concerns.

It is minimally invasive. It can be placed through a small (1.5) cm vaginal incision and even smaller incisions in the suprapubic region. It is performed under local anesthesia with sedation. It is a brief procedure and allows for same-day discharge from the hospital. The procedure does not require routine postoperative catheterization. As the dissection is less extensive than for Burch or pubovaginal sling, recovery from the procedure is faster and easier.

It is safe. The TVT and TVT-O comes with a tracking lot number for safety, and Medical Device Reporting (MDR) that is followed by the FDA. The Manufacturer and User Facility Device Experience Database (MAUDE) tracks complications, as the TVT and TVT-O are classified as medical devices. This is unlike any other treatment for stress urinary incontinence, even though both pubovaginal slings and urethropexies often use prolene sutures-the same substance as TVT mesh.

The mesh used for TVT and TVT-O is a macroporous, polypropylene, knitted mesh that is well tolerated by the body. Fibroblasts and blood vessels can easily grow into the mesh to allow collagen deposition and create a new support for the urethra. Polypropylene, used for over 40 years in humans, has been shown to be stable and non-degrading. The polypropylene used in TVT and TVT-O has not demonstrated an inflammatory response. Mesh exposures are rare, occurring in only 1-3% of patients. There is growing knowledge of risk factors that may increase the risk of exposure/erosion, and treatment of exposures/erosions is generally uncomplicated.

Complications arise from all surgical procedures designed to treat stress urinary incontinence, and mesh complications are the only complications unique to the TVT and TVT-O procedures. Other complications can occur, but are minimal for those undergoing TVT and TVT-O. Retropubic hematoma formation is rare due to the narrow design of the blunt trocars used to place the sling. Urinary retention is not common (<10%), and if it occurs it can be remedied by loosening the sling in the office. Dyspareunia is rare after a TVT and TVT-O (see above) and pain with intercourse, leakage with intercourse and fear of incontinence during sex all improve after sling placement (Zyczynski, HM, et al., Sexual activity and function in women more than 2 years after midurethral sling placement, Am J Obstet Gynecol. 2012 Nov;207(5):421.e1-6). Infection is rare, in part due to the design of the plastic sheath placed over the mesh, resulting in a more sterile procedure. Voiding dysfunction such as urinary urgency is rare (6%) and for most patients improves. Voiding dysfunction is more common with open colposuspension than with synthetic mid-urethral slings (American College of Obstetricians and Gynecologists. Obstet

Gynecol 2015; 126:e66–81).

It is effective. The success rate of TVT and TVT-O is 85-90%. This rate has lasted as long as 17 years in longitudinal follow up of some of the initial cohorts, and has been confirmed in dozens of randomized controlled trials. Mid-urethral slings are also effective in older patients, and in patient with severe incontinence such as intrinsic sphincter deficiency. As of the most recent Cochrane review, there are at least 81 trials that evaluated 12,113 women with regard to TVT sling. This degree of scrutiny makes mid-urethral slings the most studied surgical technique for the treatment of stress urinary incontinence (Cochrane Database Syst Rev. 2015 Jul 1;(7).

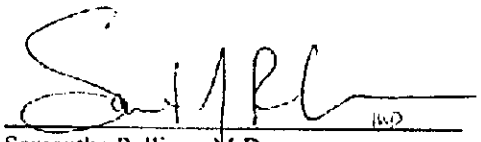
It is carefully and thoroughly taught. The TVT and TVT-O comes with instructions for use (IFU) to guide the physician in its use, application and awareness and avoidance of complications. The American Council for Graduate Medical Education, the American Urogynecologic Society and the International Urogynecologic Association all mandate education regarding mid-urethral slings for their trainees, including medical students, residents and fellows. Ethicon provides multiple opportunities for further education including webinars, monographs, in-person training on cadavers, and proctorships to ensure those providing care for women with stress urinary incontinence have ample opportunity to learn the technique and clinical care requirements for this surgical procedure. The FDA has issued a warning about the use of mesh in pelvic reconstructive surgery, though it specifically excluded the suburethral sling in its most recent statement (Urogynecologic Surgical Mesh: Update on the Safety and Effectiveness of Transvaginal Placement for Pelvic Organ Prolapse, FDA July 2011). The warning created additional awareness for the public and surgeons, and has enhanced the responsibility of each surgeon to develop expertise in the placement of mid-urethral slings if he chooses to use them. The FDA warning does not, however, diminish the fact that education and research about the use of the mid-urethral sling is greater than any other treatment for stress urinary incontinence.

Conclusion

Based upon my review of the literature, my experience as an educator, my subspecialty training in female pelvic medicine, my experience as a surgeon with TVT and TVT-O slings and many alternative treatments for stress urinary incontinence, I believe that the TVT and TVT-O slings are a reasonably safe, effective treatment for stress urinary incontinence. The design of TVT has revolutionized the treatment of female stress urinary incontinence, improving the lives of tens of thousands of women. The TVT and TVT-O procedures are characterized by their minimally invasive technique, minimal frequency of complications, ease of recovery, and reliable success for their intended purposes. Based on more scientific literature than is available for any other SUI treatment, the TVT and TVT-O are safe for their intended use, the treatment of female stress urinary incontinence. The mesh used in TVT/TVT-O has been well studied, and is safe and effective with minimal complications. The educational opportunities for surgeons to learn the technique, indications and potential complications for surgery abound, and are clear in the IFU and Professional Education materials. From this wealth of information, surgeons are able to

meet the expectations of a thorough and accurate understanding of risks, benefits and surgical technique. The benefits of TVT/TVT-O far outweigh the risks, and thus TVT/TVT-O have become the gold standard for the surgical treatment of female stress urinary incontinence.

The opinions set forth in my report are based on the information that is currently available to me. I reserve the right to modify or amend these opinions if new information becomes available.



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